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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/786,988	01/23/97	LITTLE D	U/18485-0012

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EXAMINER	
BEX, P	
ART UNIT	**PAPER NUMBER**
1743	31

DATE MAILED: 02/08/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	08/786,988	LITTLE ET AL.	
	Examiner	Art Unit	
	P. K. Bex	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9-34,40-51 and 54-94* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9-34,40-51 and 54-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *21-23,30* .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on November 28, 2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/786,988 is acceptable and a CPA has been established. An action on the CPA follows.

2. The cancellation of claims 95-99 is acknowledged and has been entered into the record.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-6, 9-34, 40-51, 54-69 and 87-93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tisone (USP 5,743,960) in view of Patterson (USP 5,869,240).

Tisone discloses a method and an apparatus for dispensing a material on a substrate substantially as claimed. The method comprises the steps of providing a vesicle 12 having an

interior chamber containing a fluid, disposing the vesicle 12 adjacent a first location on the surface of a substrate 30, controlling the vesicle to eject from the chamber a nanoLiter volume of the fluid to dispense the fluid at the first location of the surface of the substrate, and moving the vesicle to a set of positions so that fluid is dispensed from the vesicle at each location of the set for forming an array of fluid material (Figs. 1, 6-7). Note that Tisone teaches in one of the embodiments that the method can be used to dispense sample fluids onto a diagnostic test strip for testing (column 11, lines 14-25). Tisone does not specifically recite the step of performing mass spectrometry analysis for the material. However, such an analysis step on a substrate using a mass spectrometer is considered conventional in the art, see Patterson. Patterson teaches a method for sequencing polymers using a mass spectrometer in order to provide a rapid, automated and cost effective sequencing of polymers with a statistical certainty (Background and Summary of the Invention sections).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided the method and apparatus of Tisone et al. with a spectrometer, as taught by Patterson, in order to provide a rapid, automated and cost effective sequencing of polymers with a statistical certainty.

6. Claims 70-86 and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ershow et al. (USP 5,756,050) in view of Patterson (USP 5,869,240).

Ershow et al. disclose a method for dispensing nanoLiter volumes of a material on the surface of a substrate 16 substantially as claimed. The method comprises the steps of providing a pin assembly 1 having a plurality of elongated vesicles 2 arranged as an array for dispensing a liquid therefrom (Figs. 1-2), wherein each vesicle comprises a solid shaft of material having an

end for retaining a nanoLiter volume for fluid; loading a volume of fluid from a fluid source 14 onto the end of the vesicles; disposing the pin assembly to align the vesicles at a first set of locations adjacent to the surface of the substrate 16; and contacting the loading fluid to the surface of the substrate is formed (Figs. 3-4). Ershow et al. fail to specifically recite a diagnostic tool comprising a mass spectrometer. However, the use of such a spectrometer for identifying polymers is considered conventional in the art, see Patterson (USP 5,869,240). Paterson teaches a method for sequencing polymers using a mass spectrometer in order to provide a rapid, automated and cost effective sequencing of polymers with statistical certainty (Background and Summary of the Invention sections).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided the method of Ershow et al. with a spectrometer, as taught by Patterson, in order to provide a rapid, automated and cost effective sequencing of polymers with a statistical certainty.

Response to Arguments

7. Applicant's arguments filed November 28, 2000 and the declaration under 37 CFR 1.132 filed May 12, 2000 have been fully considered but they are not persuasive.

Applicants argue that the declaration demonstrates that the use of nanoLiter volumes to produce arrays for analysis by mass spectrometry confers unexpected increase in reproducibility and accuracy not taught or suggested by Tisone (USP 5,743,960), Patterson (USP 5,869,240) or Ershow et al. (USP 5,756,050). However, the declaration and review article specify improved results in mass spectrometric analysis by forming an array from about 300 picoLiter drops, wherein 15-20 drops are dispensed into each array element, forming 4.5-6 nanoLiter volume

array elements. The specific use of picoLiter droplets provides for rapid evaporation and crystallization of the sample to be detected. The declaration and review article indicate that the mass spectrometric analysis of these arrays is improved over the prior art, which teaches hundred nanoLiter volume array elements. This argument is not germane to the issue since applicant has not restricted that claims to anything but nanoLiter volume array elements, which appears to read on the prior art.

Applicants argue that Tisone does not teach or suggest, of all possible available technologies, which type of analytical technology can be used to analyze the sample transferred by the aspirating operation. Applicants further argue that Tisone does not teach that such a sample can be analyzed by mass spectrometry. The arguments are not persuasive. Firstly, the teaching of all available technologies is irrelevant to the issue because the claimed dispensing methods are clearly taught by Tisone. Secondly, Patterson which the Examiner relies on teaches the mass spectrometry.

With respect to the Patterson reference, Applicants contend that Patterson does not teach combining mass spectrometric analysis with arrays of samples produced by dispensing a nanovolume, nor that it is advantageous to perform mass spectrometry on an array of samples of a size that results from dispensing nanoLiter volumes of material on a substrate. In response to Applicants' arguments against the reference individually, one cannot show non obviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants' further argues that the combination of teachings of the cited references do not teach or suggest the unexpected results that derive from using arrays produced by dispensing nanoLiter volumes of samples for mass spectrometric analysis. This argument is not persuasive because the claimed use of a nanoLiter volume of sample is clearly taught by Tisone. Further, one of ordinary skill in the art would recognize that such a low volume of sample dispensing offers several advantages such as, dispensed volume accuracy and uniformity, as well as elimination of wasting expensive samples or reagents, etc.

Conclusion

8. No claims allowed.

9. This is a continuation of applicant's earlier Application No. 08/786,988. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however,

event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Kathryn Bex whose telephone number is (703) 306-5697. The examiner can normally be reached on Mondays-Thursdays from 7:30 am to 5:00 pm EST.

The fax number for the organization where this application or proceeding is assigned is (703) 305-7718 for official papers prior to mailing of a Final Office Action. For official papers after mailing of a Final Office Action, use fax number (703) 305-3599. For unofficial or draft papers use fax number (703) 305-7719. Please label all faxes as official or unofficial. The above fax numbers will allow the paper to be forwarded to the examiner in a timely manner.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0661.

Kath Bex

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